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PATENT AND TRADEMARK OFFICE

#10  
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In re Application of:

KAZUHIKO TAKE ET AL.

Serial No.: 09/857,869

Art Unit 1624

Filed: June 12, 2001

EXAMINER: EMILY BERNHARDT

For: PIPERAZINE DERIVATIVES

DECLARATION

I, MASAHIKO MATSUO, a citizen of Japan residing at 4-56-7, Keyakidai, Sanda-shi, Hyogo, Japan, declare and say that:

I graduated from Kobe University, in March 1981 and completed the master course of Department of Science at Kobe University in March 1983;

Since April 1983, I have been as a pharmacologist, in the continuous employ of Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan and now a senior manager of the Medicinal Biology Research Laboratories;

I received the Ph. D. Degree of Pharmacology, in 1997 from Osaka University;

I am a member of the Japanese Pharmacological Society; and

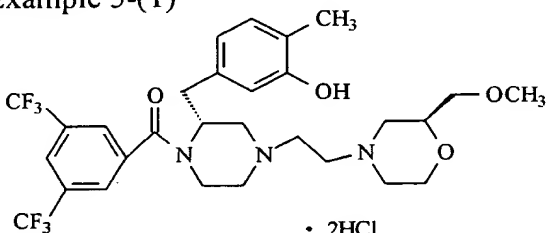
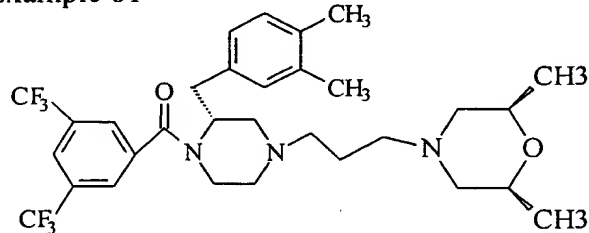
I received from Dr. Kazuhiko Take Test Compounds Example 5-(1) and Example 81 and have measured their capability of h-NK<sub>1</sub> receptor binding.

The test result obtained is described in detail hereinafter.

Comparison between a representative compound (Example 5-(1))  
of the present invention and Example 81 selected by the Examiner in WO ' 597  
as their capability of h-NK<sub>1</sub> receptor binding

Test method: the same as the test method described in the present application,  
pages 24 -26

Test Results

|                        | Test Compounds                                                                                                | Capability of h-NK <sub>1</sub><br>receptor binding<br>IC <sub>50</sub> |
|------------------------|---------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Present<br>application | Example 5-(1)<br><br>• 2HCl | $0.88 \times 10^{-9} \text{ M}$                                         |
| WO ' 597               | Example 81<br><br>• 2HCl  | $4.89 \times 10^{-9} \text{ M}$                                         |

no  
negat  
compd  
for test

This result demonstrates that the binding capability  
(affinity) of the representative compound, Example 5-(1), in the  
present invention is more than 5 times (5.6 times) as strong as  
that of the compound of Example 81 in WO ' 597.

It is declared by the undersigned that all statements made

herein of undersigned's own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

A handwritten signature in cursive script, appearing to read "M. Matsuo", is written over a horizontal line.

Masahiko Matsuo

This *8th* day of January, 2003

Osaka, Japan